

REMARKS

The amendment to the Specification merely adds a specific claim of priority to the priority documents to the present International Application, U.S. Provisional Applications 60/146,181, 60/146,181 and 60/172,601, as required under 35 U.S.C. 119(e)(1).

The amendment to Claim 6 and new Claims 7 and 8 are merely mechanical amendments to eliminate the multiple dependency of the original claims.

New Claims 9-20 more particularly point out and distinctly claim the subject matter Applicants regard as their invention. No new matter is added to the specification.

New Claims 9 and 10 are drawn to another preferred method of treatment using the presently claimed novel compounds, and finds support throughout the specification and specifically at page 3, lines 17-32, especially lines 27-28.

New Claims 11-20 are drawn to various preferred embodiments of the inventive family of compounds and are supported throughout the specification, and especially as follows:

New Claim 11, see page 8, lines 23-24;

New Claim 12, see page 8, line 27;

New Claim 13, see page 8, line 27 and page 10, line 17;

New Claim 14, see page 6, lines 5-6, and example 4;

New Claim 15, see page 9, line 25, and example 4;

New Claim 16, see page 10, line 15-16, and example 5;

New Claim 17, see examples 43, 4, 7, and 28;

New Claim 18, see page 8, lines 28-31;

New Claim 19, see page 8, lines 28-29, page 9, lines 24 and 27, page 10, lines 22-23, and example 34;

New Claim 20, see example 48;

A mark-up copy of Claim 6 showing the changes made in this present amendment is enclosed on a separate sheet as required by 37 C.R.F. 1.121. A clean copy of the entire

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claim set as amended herewith is also enclosed for the Examiner's convenience. Entry of the forgoing amendments prior to substantive examination is respectfully requested.

Respectfully submitted,



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MARKED-UP COPY OF AMENDED CLAIMS

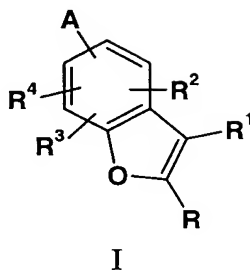
6. The [A] method of [any of] Claim[s] 3[, 4, or 5] where the mammal is human.

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We Claim:

1. The compounds of Formula I:



where:

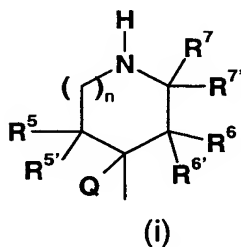
R is hydrogen, halo, trifluoromethyl or C₁-C₆ alkyl;

R¹ is hydrogen, halo, trifluoromethyl, phenyl, or C₁-C₆ alkyl;

R², R³, and R⁴ are independently hydrogen, halo, trifluoromethyl, cyano, C₁-C₄ alkoxy, C₁-C₄ alkoxycarbonyl, C₁-C₆ alkyl, C₁-C₆ alkyl substituted with a substituent selected from the group consisting of C₁-C₄ alkoxy and hydroxy, or -C(O)NHR⁹;

R⁹ is C₁-C₈ alkyl where the alkyl chain is optionally substituted with a substituent selected from the group consisting of phenyl and pyridyl;

A is attached at either the 4- or 7-position of the benzofuran nucleus and is an amine of formula:



n is 0, 1, or 2;

R⁵, R⁶, and R⁷ are independently hydrogen or C₁-C₄ alkyl;

Q is hydrogen;

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$R^{5'}$ is hydrogen or methyl, provided that $R^{5'}$ may be methyl only when R^5 is other than hydrogen, or $R^{5'}$ and Q taken together with the carbon atoms to which they are attached form a double bond;

$R^{6'}$ is hydrogen or methyl, provided that $R^{6'}$ may be methyl only when R^6 is other than hydrogen, or $R^{6'}$ and Q taken together with the carbon atoms to which they are attached form a double bond;

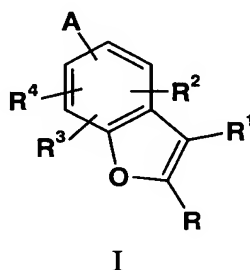
$R^{7'}$ is hydrogen or methyl, provided that $R^{7'}$ may be methyl only when R^7 is other than hydrogen;

or pharmaceutically acceptable acid addition salts thereof subject to the following provisos:

a) when n is 1 or 2, at least one of R^5 , R^6 , and R^7 , must be other than hydrogen; and

b) no more than two of R^5 , $R^{5'}$, R^6 , $R^{6'}$, R^7 , and $R^{7'}$ may be other than hydrogen.

2. A pharmaceutical formulation which comprises, in association with a pharmaceutically acceptable carrier, diluent or excipient, a compound of Formula I:



where:

R is hydrogen, halo, trifluoromethyl or C_1 - C_6 alkyl;

R^1 is hydrogen, halo, trifluoromethyl, phenyl, or C_1 - C_6 alkyl;

R^2 , R^3 , and R^4 are independently hydrogen, halo, trifluoromethyl, cyano, C_1 - C_4 alkoxy, C_1 - C_4 alkoxy carbonyl, C_1 - C_6 alkyl, C_1 - C_6 alkyl substituted with a

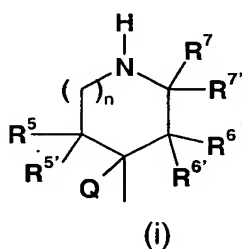
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substituent selected from the group consisting of C₁-C₄ alkoxy and hydroxy, or -C(O)NHR⁹;

R⁹ is C₁-C₈ alkyl where the alkyl chain is optionally substituted with a substituent selected from the group consisting of phenyl and pyridyl;

A is attached at either the 4- or 7-position of the benzofuran nucleus and is an amine of formula:



n is 0, 1, or 2;

R⁵, R⁶, and R⁷ are independently hydrogen or C₁-C₄ alkyl;

Q is hydrogen;

R^{5'} is hydrogen or methyl, provided that R^{5'} may be methyl only when R⁵ is other than hydrogen, or R^{5'} and Q taken together with the carbon atoms to which they are attached form a double bond;

R^{6'} is hydrogen or methyl, provided that R^{6'} may be methyl only when R⁶ is other than hydrogen, or R^{6'} and Q taken together with the carbon atoms to which they are attached form a double bond;

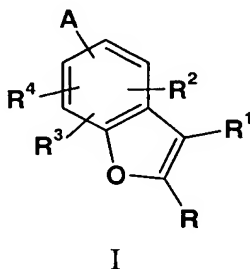
R^{7'} is hydrogen or methyl, provided that R^{7'} may be methyl only when R⁷ is other than hydrogen;

or pharmaceutically acceptable acid addition salts thereof subject to the following provisos:

a) when n is 1 or 2, at least one of R⁵, R⁶, and R⁷, must be other than hydrogen; and

b) no more than two of R⁵, R^{5'}, R⁶, R^{6'}, R⁷, and R^{7'} may be other than hydrogen.

3. A method for increasing activation of the 5-HT_{2C} receptor in mammals, comprising administering to a mammal in need of such activation a pharmaceutically effective amount of a compound of Formula I:



where:

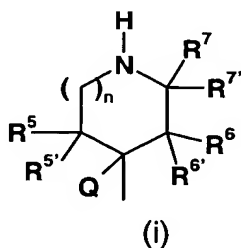
R is hydrogen, halo, trifluoromethyl or C₁-C₆ alkyl;

R¹ is hydrogen, halo, trifluoromethyl, phenyl, or C₁-C₆ alkyl;

R², R³, and R⁴ are independently hydrogen, halo, trifluoromethyl, cyano, C₁-C₄ alkoxy, C₁-C₄ alkoxycarbonyl, C₁-C₆ alkyl, C₁-C₆ alkyl substituted with a substituent selected from the group consisting of C₁-C₄ alkoxy and hydroxy, or -C(O)NHR⁹;

R⁹ is C₁-C₈ alkyl where the alkyl chain is optionally substituted with a substituent selected from the group consisting of phenyl and pyridyl;

A is attached at either the 4- or 7-position of the benzofuran nucleus and is an amine of formula:



n is 0, 1, or 2;

R⁵, R⁶, and R⁷ are independently hydrogen or C₁-C₄ alkyl;

Q is hydrogen;

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$R^{5'}$ is hydrogen or methyl, provided that $R^{5'}$ may be methyl only when R^5 is other than hydrogen, or $R^{5'}$ and Q taken together with the carbon atoms to which they are attached form a double bond;

$R^{6'}$ is hydrogen or methyl, provided that $R^{6'}$ may be methyl only when R^6 is other than hydrogen, or $R^{6'}$ and Q taken together with the carbon atoms to which they are attached form a double bond;

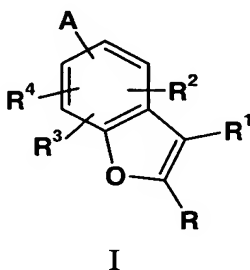
$R^{7'}$ is hydrogen or methyl, provided that $R^{7'}$ may be methyl only when R^7 is other than hydrogen;

or pharmaceutically acceptable acid addition salts thereof subject to the following provisos:

a) when n is 1 or 2, at least one of R^5 , R^6 , and R^7 , must be other than hydrogen; and

b) no more than two of R^5 , $R^{5'}$, R^6 , $R^{6'}$, R^7 , and $R^{7'}$ may be other than hydrogen.

4. A method for the treatment of obesity in mammals, comprising administering to a mammal in need of such activation a pharmaceutically effective amount of a compound of Formula I:



where:

R is hydrogen, halo, trifluoromethyl or C_1 - C_6 alkyl;

R^1 is hydrogen, halo, trifluoromethyl, phenyl, or C_1 - C_6 alkyl;

R^2 , R^3 , and R^4 are independently hydrogen, halo, trifluoromethyl, cyano, C_1 - C_4 alkoxy, C_1 - C_4 alkoxy carbonyl, C_1 - C_6 alkyl, C_1 - C_6 alkyl substituted with a

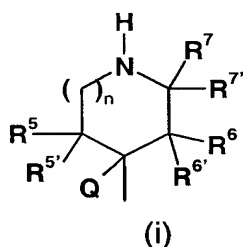
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substituent selected from the group consisting of C₁-C₄ alkoxy and hydroxy, or -C(O)NHR⁹;

R⁹ is C₁-C₈ alkyl where the alkyl chain is optionally substituted with a substituent selected from the group consisting of phenyl and pyridyl;

A is attached at either the 4- or 7-position of the benzofuran nucleus and is an amine of formula:



n is 0, 1, or 2;

R⁵, R⁶, and R⁷ are independently hydrogen or C₁-C₄ alkyl;

Q is hydrogen;

R^{5'} is hydrogen or methyl, provided that R^{5'} may be methyl only when R⁵ is other than hydrogen, or R^{5'} and Q taken together with the carbon atoms to which they are attached form a double bond;

R^{6'} is hydrogen or methyl, provided that R^{6'} may be methyl only when R⁶ is other than hydrogen, or R^{6'} and Q taken together with the carbon atoms to which they are attached form a double bond;

R^{7'} is hydrogen or methyl, provided that R^{7'} may be methyl only when R⁷ is other than hydrogen;

or pharmaceutically acceptable acid addition salts thereof subject to the following provisos:

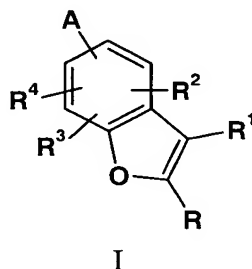
a) when n is 1 or 2, at least one of R⁵, R⁶, and R⁷, must be other than hydrogen; and

b) no more than two of R⁵, R^{5'}, R⁶, R^{6'}, R⁷, and R^{7'} may be other than hydrogen.

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5. A method for the treatment of depression in mammals, comprising administering to a mammal in need of such activation a pharmaceutically effective amount of a compound of Formula I:



where:

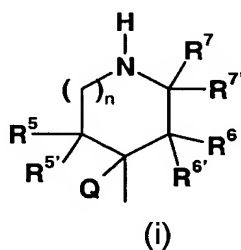
R is hydrogen, halo, trifluoromethyl or C₁-C₆ alkyl;

R¹ is hydrogen, halo, trifluoromethyl, phenyl, or C₁-C₆ alkyl;

R², R³, and R⁴ are independently hydrogen, halo, trifluoromethyl, cyano, C₁-C₄ alkoxy, C₁-C₄ alkoxycarbonyl, C₁-C₆ alkyl, C₁-C₆ alkyl substituted with a substituent selected from the group consisting of C₁-C₄ alkoxy and hydroxy, or -C(O)NHR⁹;

R⁹ is C₁-C₈ alkyl where the alkyl chain is optionally substituted with a substituent selected from the group consisting of phenyl and pyridyl;

A is attached at either the 4- or 7-position of the benzofuran nucleus and is an amine of formula:



n is 0, 1, or 2;

R⁵, R⁶, and R⁷ are independently hydrogen or C₁-C₄ alkyl;

Q is hydrogen;

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$R^{5'}$ is hydrogen or methyl, provided that $R^{5'}$ may be methyl only when R^5 is other than hydrogen, or $R^{5'}$ and Q taken together with the carbon atoms to which they are attached form a double bond;

$R^{6'}$ is hydrogen or methyl, provided that $R^{6'}$ may be methyl only when R^6 is other than hydrogen, or $R^{6'}$ and Q taken together with the carbon atoms to which they are attached form a double bond;

$R^{7'}$ is hydrogen or methyl, provided that $R^{7'}$ may be methyl only when R^7 is other than hydrogen;

or pharmaceutically acceptable acid addition salts thereof subject to the following provisos:

a) when n is 1 or 2, at least one of R^5 , R^6 , and R^7 , must be other than hydrogen; and

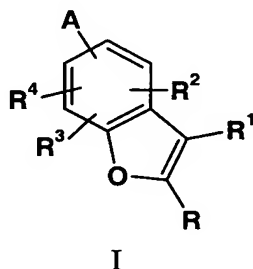
b) no more than two of R^5 , $R^{5'}$, R^6 , $R^{6'}$, R^7 , and $R^{7'}$ may be other than hydrogen.

6. (Amended) The method of Claim 3 where the mammal is human.

7. (new) The method of Claim 4 where the mammal is human.

8. (new) The method of Claim 5 where the mammal is human.

9. (new) A method for the treatment of obsessive compulsive disorder in mammals, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula I:



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where:

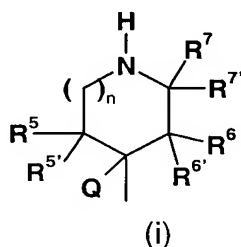
R is hydrogen, halo, trifluoromethyl or C₁-C₆ alkyl;

R¹ is hydrogen, halo, trifluoromethyl, phenyl, or C₁-C₆ alkyl;

R², R³, and R⁴ are independently hydrogen, halo, trifluoromethyl, cyano, C₁-C₄ alkoxy, C₁-C₄ alkoxycarbonyl, C₁-C₆ alkyl, C₁-C₆ alkyl substituted with a substituent selected from the group consisting of C₁-C₄ alkoxy and hydroxy, or -C(O)NHR⁹;

R⁹ is C₁-C₈ alkyl where the alkyl chain is optionally substituted with a substituent selected from the group consisting of phenyl and pyridyl;

A is attached at either the 4- or 7-position of the benzofuran nucleus and is an amine of formula:



n is 0, 1, or 2;

R⁵, R⁶, and R⁷ are independently hydrogen or C₁-C₄ alkyl;

Q is hydrogen;

R^{5'} is hydrogen or methyl, provided that R^{5'} may be methyl only when R⁵ is other than hydrogen, or R^{5'} and Q taken together with the carbon atoms to which they are attached form a double bond;

R^{6'} is hydrogen or methyl, provided that R^{6'} may be methyl only when R⁶ is other than hydrogen, or R^{6'} and Q taken together with the carbon atoms to which they are attached form a double bond;

R^{7'} is hydrogen or methyl, provided that R^{7'} may be methyl only when R⁷ is other than hydrogen;

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or pharmaceutically acceptable acid addition salts thereof subject to the following provisos:

a) when n is 1 or 2, at least one of R⁵, R⁶, and R⁷, must be other than hydrogen; and

b) no more than two of R⁵, R^{5'}, R⁶, R^{6'}, R⁷, and R^{7'} may be other than hydrogen.

10. (new) The method of Claim 9 where the mammal is human.

11. (new) A compound of Claim 1 where A is attached at the 7-position of the benzofuran nucleus.

12. (new) A compound according to Claim 11 where Q is hydrogen.

13. (new) A compound according to Claim 12 where R⁶ is C₁-C₄ alkyl and R⁵, R^{5'}, R⁷ and R^{7'} are each hydrogen.

14. (new) A compound according to Claim 13 where R^{6'} is hydrogen, and R⁶ and the benzofuran core are in the cis configuration with regard to each other.

15. (new) A compound according to Claim 13 where R⁶ is methyl.

16. (new) A compound according to Claim 13 where R^{6'} is methyl.

17. (new) A compound according to Claim 15 which is 3-methyl-4-(benzofur-7-yl)-piperidine, 3-methyl-4-(5-fluorobenzofur-7-yl)-piperidine, 3-methyl-4-(6-fluorobenzofur-7-yl)-piperidine, or 3-methyl-4-(5,6-difluorobenzofur-7-yl)-piperidine.

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18. (new) A compound according to Claim 11 where one of $R^{5'}$ and Q, or $R^{6'}$ and Q, taken together with the carbon atoms to which they are attached form a double bond.

19. (new) A compound according to Claim 18 where of $R^{5'}$ and Q, taken together with the carbon atoms to which they are attached form a double bond, $R^{6'}$ is C_1 - C_4 alkyl, and $R^{6'}$ is methyl.

20. (new) A compound according to Claim 18 which is 2-methyl-4-(4-trifluoromethylbenzofur-7-yl)-1,2,3,6-tetrahydropyridine.